The Role of Stem Cell in Plastic Reconstructive and Aesthetic Surgery

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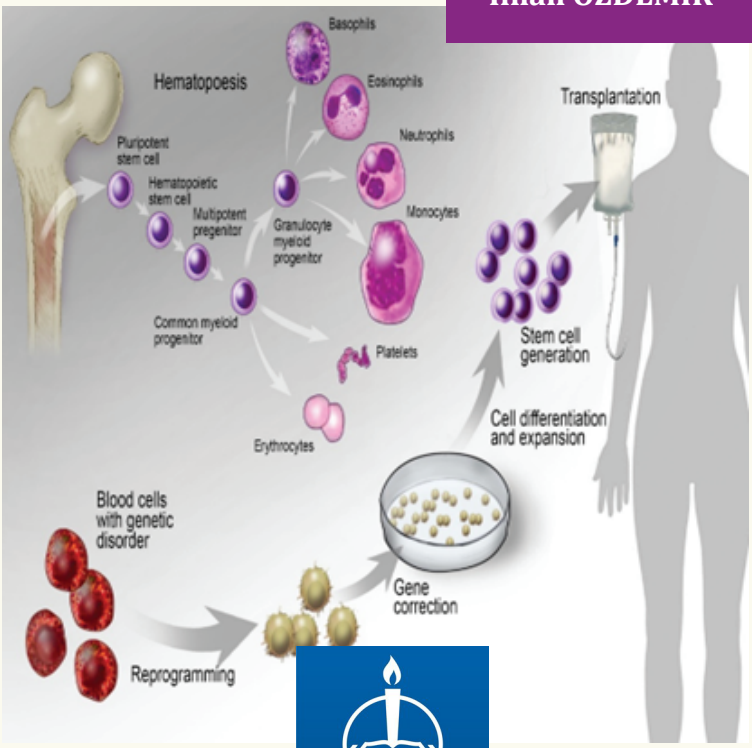

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PREFACE

Can evaluate stem cell applications in two main groups in terms of Plastic Reconstructive and Aesthetic Surgery. The first of these is aesthetic applications. Stem cell applications have significant potential, especially in the rejuvenation phase of the skin. Oil injection applications enriched with stem cells are a more effective treatment method for removing the aged appearance of face and hand skin. In fillings made with non-natural products such as implants, up to 70% of the filler is reabsorbed by the body. And the body may show allergic reactions to these artificial substances. However, with the fillings made with the use of regenerative cells taken from the person's own body, this problem is minimized and a more natural and permanent youthful appearance is achieved, away from artificiality. Therefore, one-time injections with regenerative cells are effective instead of repeated operations. In addition, the second application area in Plastic Reconstructive and Aesthetic Surgery is a group of diseases in which skin and subcutaneous tissue changes due to non-healing wounds, blood supply disorders or radiotherapy applications are really difficult for medicine. Pressure sores (bed sores) are skin and/or subcutaneous tissue damage, usually over bony prominences, caused by pressure alone or by friction and

pressure. In bed (or chair) dependent patients, pressure is placed on soft tissues due to the pressure created by body weight. The blood circulation in these tissues, which are stuck between the bone protrusion and the bed, is disturbed and eventually the tissues are damaged. With stem cell applications, vascularization in the area of the wounds, and therefore circulation in the area, is increased, the immune system is stimulated and supported, thereby accelerating the regeneration of tissues. Thus, stem cells are among the treatment methods in plastic surgery with many aspects, and more comprehensive studies are needed to create a better model in the future.

CONTENTS

INTRODUCTION

All organs and tissues in the human body are made up of cells. Some cells are capable of renewing themselves and transforming into different cell types. These cells, called stem cells, can divide and reproduce, unlike muscle and nerve cells that cannot reproduce. The stem cell, which enables the formation of hundreds of thousands or even millions of cells from a single cell, can also reproduce by dividing in order to renew itself. Although stem cells cannot provide oxygen transport, hormonal and neural transmission, they play a role in the formation of cells that must fulfill these vital functions. The stem cell, which has the ability to renew itself for a lifetime, transforms into other cells. It differentiates in line with the needs of the body and ensures the development, maturation and proliferation of other cells. However, as age progresses, the amount of blood cells in the body decreases compared to other cells. While 1 out of 10 thousand cells in newborn babies is a stem cell, in a 65-year-old person, only 1 out of 1 million cells is a stem cell. Damaged tissues and organs become irreparable due to the decrease in the amount of stem cells with aging. Therefore, stem cell therapy is very important in the treatment of many diseases that may result in death, some types of cancer and congenital blood diseases. Stem

cell is the name given to undifferentiated cells that can renew themselves by continuing to divide for a very long time in the body of a living thing and thus create differentiated cells. In other words, cells that have the potential to transform into different cell types and renew themselves are called stem cells. The targets of the cells in our body such as muscle, liver and skin cells are certain, and when these cells divide, they form a cell like themselves. However, stem cells do not have a defined function different from these cells. Therefore, they can transform into different cell types according to the signals they receive. The most important factors determining this are genes and external stimuli. When death or damage occurs in any cell group in our body, stem cells transform into whichever cell is needed. The zygote that emerges by the union of the sperm and the ovum alone has the genetic information and power to form the whole organism. This is the first embryonic cell that has the potential to transform into all cells, called a "totipotent" cell. In the first 4-5 days following fertilization, these cells have the same power and are capable of forming an organism on their own. The cell mass formed after approximately 5 days, that is, after 2-3 divisions, is called blastocyst, and the cells within this mass (inner cell mass) have the ability to transform into all cells in the body. However, these cells alone cannot form an organism. For this reason, these cells

are called “puliripotent” cells. After this stage, the cells have more specific functions and form adult stem cells. These stem cells, which are a little more specialized, are called "multipotent" cells. The best example of this is the hematopoietic stem cells found in the bone marrow both in childhood and adulthood. These cells, which can only transform into a few cell types in the human body, can transform into many more cell types when the necessary supportive environment and signals are provided under laboratory conditions. In the light of this information, the question that has been asked throughout the history of humanity has come to the fore again: “Is there a better way to restore the functions of a damaged organ than to replace it with a new one? ›r? “

Throughout history, the thought of transplantation has focused on this question, and sphinxes, mermaids, and centaurs have taken their place in mythology as examples of xenotransplantation. In mythology, the story of Prometheus, who was punished by Zeus after stealing fire from Mount Olympus, from the gods, and gifting it to humanity, is an example of this. The liver of Prometheus, who was punished by Zeus by being tied to a rock in the Caucasus (Kaf) Mountain, in the form of his liver being eaten by an eagle every day, renews itself every day. This is the first story that reveals the regeneration ability of the liver cell and

therefore the concept of stem cell. Centuries later, this transplantation fantasy and technology, in the hands of a medical professional, became the material for Mary Shelley's Frankenstein, an extreme example of classical literature. Prof. Dr. Süreyya Tahsin Aygün is the researcher who made perhaps the first studies in the world on today's stem cell therapy and said that the way to prolong human life is in the placentas and cord cells expelled after birth. In the 1950s-1960s, he conducted research in the treatment of various diseases with fetal grafts and cord blood grafts in animals and published them in German medical journals. The propagation of embryonal carcinoma cells in culture, first described in 1967, is also an important step forward in this field, and since then, more than human and mouse teratocarcinomas have been identified. a large number of cell lines have been described. The differentiation of these cells; It develops by cell aggregation resulting in the formation of embryo-like formations called embryoid bodies. These embryoid bodies were first observed in acid fluids of mice with embryonal carcinoma. These cells also appear to constitute an important model for developmental biologists, because their in-vitro differentiation patterns explain various aspects of embryogenesis and result in the formation of cells representative of all 3 germ layers. In the same time period; Studies have also begun on the production of

human embryonic stem cells using excess embryos taken from in vitro fertilization clinics. These studies were initially unsuccessful, but rabbit embryo cells were brought into culture in an attempt to study differentiation in cells isolated from pre-implantation blastocysts. In 1998, the first human embryonic stem cells were cultured. In the same time period, embryonic germ cells were obtained from human primordial germ cells . While the possibility of using these stem cells for disease treatment in the future creates great excitement, unsolved ethical issues have created serious resistance. As a result of the ethical reactions shown against these cells, studies on adult stem cells have also intensified, and the apparent plasticity of these cells has led to titles such as "bone marrow to muscle", "brain to blood conversion", "blood to brain conversion". n caused. After these initial studies, numerous publications on adult and embryonic stem cells have emerged. All of these have the same purpose: “It is a stem cell-based treatment (1).

STEM CELL PLASTICITY

Basically, the principles that make up the definition of true stem cell are: 1- The ability to self-renew or the ability to generate at least one similar cell with the characteristics of the original cell (self-renewal), 2- The ability to differentiate from a single cell to

more than one series cell (multi-lineage differentiation) , 3-In-vivo functional reconstruction of a particular tissue (2). Embryonic stem cells (ESCs), derived first from mice and later from non-human primates, and much more recently from human blastocysts, follow all of these basic principles. The majority of adult stem cells meet these criteria, although their self-renewal and differentiation potential is lower than that of embryonic stem cells. Hematopoietic stem cells (HSCs), the most well-studied adult stem cells, undergo self-renewing cell divisions, at least in vivo, can differentiate into all mature blood elements at the single-cell level, and are capable of being myeloablated from a human or animal. It can repopulate the bone marrow of Other adult stem cells have been identified more recently and therefore have been less studied. However, neuronal stem cells (NKC), mesenchymal stem cells (MSC) and epidermal stem cells comply with the basic criteria described above. Corneal stem cells and other stem cells called angioblasts or endothelial stem cells also comply with these criteria, apart from their ability to differentiate into a single differentiated cell type (3). In recent years; The number of studies reporting that cells taken from a certain tissue show the ability to differentiate into a different tissue has gradually increased, and these studies have been gathered under the umbrella of "stem cell plasticity". Stem cell plasticity; It

describes the ability of a cell to differentiate into tissues other than the tissues from which it originated. Examples of this include bone marrow-derived cells that can differentiate into endothelium, muscle cells, heart muscle, and hepatocytes, and even purified hematopoietic stem cells.

Cells in the living body that can regenerate themselves and have the ability to differentiate into many cells suitable for the body's needs are defined as "Stem Cells". Undifferentiated stem cells, unlike other cells, have the characteristic features of the original cell, they have the ability to form a cell similar to each other (self-renewal) and the ability to differentiate from a single cell to more than one cell line (multilineage differentiation) (4). Although stem cells can form the basic structure of most tissues according to the signal they receive through genes, they cannot fulfill the function of specialized cells that have a specific task (for example, nerve cells, muscle cells, secretory epithelial cells, etc.). It was determined by Okarma (4) that embryonic stem cell lines proliferated during 300-400 cycles. Unlimited cleavage abilities occur through telomerase enzyme activity (5). The telomere chain is located at the end of the DNA helix, which controls the ability of cells to divide. In stem cells, the telomere chain is quite long and accordingly, telomerase enzyme activity is high. Thus, stem

cells can reproduce for a very long time by self-replication (5). One of the most important features that distinguishes stem cells from other cells is their high differentiation capacity. A series of changes that the cells that have come together to form multicellular organisms undergo in order to acquire a specific structure and undertake specific tasks is defined as "differentiation". Stem cells have important roles in the production and repair events in the organism with their differentiation potential (6).

1. Stem Cells According to Differentiation Potential Stem cells are basically defined under 3 groups as totipotent, pluripotent and multipotent.

1.1 Totipotent Stem Cells The zygote is the first embryonic stem cell that has the ability to differentiate into all the cells in the structure of the living thing, and these cells are called “totipotent cells” (Totus- full, undivided; potentia means power). Totipotent property is also valid for all cells defined as blastomere formed by division of the zygote. In addition, these stem cells, which have features such as forming placental structures (outer cell mass and trophectoderm) and differentiating into all tissues (with inner cell mass), have the capacity to regenerate living things in the early embryonic period. These cells can differentiate into all cell types

that can form a functional living thing from scratch. However, they also have the potential to transform into non-embryonic tissues such as the amniotic sac and placenta. Totipotent stem cells in advanced stages of development; they can differentiate into pluripotent stem cells (4).

1.2. Pluripotent Stem Cells are the cells found in the embryo in the blastocyst phase, which is formed on the 5th day of the preimplantation period after fertilization. blastocyst; It consists of three structures: trophoblast cells, blastocoele and inner cell mass. Pluripotent stem cells; They are cells derived from the inner cell mass that originates embryonic stem cells. It is similar to totipotent stem cells in that it can form all tissues and organs in living things. However, they cannot form placental structures and accordingly they cannot create a new living thing. However, these cells have the potential to transform into approximately 200 cell types when the necessary environment is provided (7).

1.3. Multipotent Stem Cells are cells that belong to a later stage of embryonic development, they turn into adult stem cells and can differentiate into specialized cell types. Multipotent stem cells (MSCs) are a group of stem cells that can differentiate into all blood cells and various cells specific to many organs starting from the 16th day in the human embryo body and from the 4th month

in the intrauterine stage (5). MSCs are cells that belong to a single germ leaf found in the tissues of adults and can differentiate into cell groups close to each other. MSC was first identified from the bone marrow by Friedenstein et al. (8).

SOURCES OF STEM CELLS ACCORDING TO THE TISSUES AND ORGANS THEY ARE OBTAINED

Stem cells; It can be obtained from embryonic and non-embryonic stem cells. Non-embryonic stem cells can be obtained from fetal stem cells, cadaver, umbilical cord, placenta, bone marrow, adipose tissue, stem cells found in many organs (somatic stem cells) or cells formed by transforming any cell into stem cell by differentiation in recent years. Today, especially embryonic and adult stem cells are used especially for regenerative medicine applications. Totipotent embryonic stem cells with multiple different potentials; It is very suitable for regenerative medicine applications. However, there are many ethical barriers to obtaining and using these cells. On the other hand, adult stem cells are both immunologically unproblematic and do not pose ethical problems (9). There are also stem cell sources in the body of an adult creature. Adult stem cells are undifferentiated cells found in differentiated tissues. These cells, which are found in

living things of all ages, can renew themselves and turn into different cell types when needed. These cells serve as spare parts that produce new ones instead of cells that age, degenerate or die in the tissues they are in (10). It is found in many tissues in the human body, such as bone marrow, skeletal muscle, eye, umbilical cord, nerve, liver, dental pulp and skin. Since organ-specific stem cells are in small quantities in the body, their isolation poses a separate problem and they do not have the ability to proliferate as much as embryonic stem cells, except in vivo (in-vivo environment). adult stem cells; It has the feature of multipotent mesenchymal stem cells and its development capacity is less than embryonic stem cells, but their tissue-specific differentiation is an important feature that distinguishes these stem cells from other stem cells (11). He defined satellite cells located just below the basement membrane of the muscle cell as adult stem cells of muscle tissue (12). These definitions were the first classification of adult stem cells. After that, studies gained momentum at the end of the 1960s, bone marrow mesenchymal stem cells (MSCs); Adult hematopoietic stem cells and neural stem cells were found in cord blood (13). Many studies on adult stem cells have focused on bone marrow derived stem cells. Human bone marrow originates from the embryonic mesoderm. Bone marrow cells mainly consist of two cell groups; these are

hematopoietic stem cells and MSCs with supporting properties. The stromal cell group in question in both experimental animals and humans consists of heterogeneous cell groups, and one of these groups is a group of cells called MSC. which Friedenstein et al. defined as the fibroblast colony-forming cell group (CFU-F); MSCs, which are non-hematopoietic bone marrow progenitors, have now been included in the scope of Cell Drug by the European Union (EU) medical agency, especially due to its regenerative and immunoregulatory effects (14). Adipose tissue contains more MSC when compared to bone marrow, peripheral blood and cord blood. Multipotent stem cells from adipose tissue were first reported by Zuk et al. (15) and defined as adipose tissue-derived stem cells. MSC can be isolated from the synovial membrane, skeletal muscle, dermis, pericyte, cartilage, tendon, trabecular bone, umbilical cord, lung, dental pulp, amniotic fluid, fetal liver, and peripheral blood, except for bone marrow and adipose tissue (15). 3. Adult Stem Cells MSCs, which are adult stem cells, are multipotent. Thanks to MSCs having stromal origin; In general, they increase the possibility of application in many fields of medicine with their "support cell" feature. They are durable cells that can be isolated from many tissues and are suitable for multiplication. They constitute approximately 0.01% to 0.001% of bone marrow cells. Studies have differentiated

MSCs into adipocyte, chondrocyte, myoblast and osteoblast cells. MSCs, regardless of the tissue from which they were obtained, have many features such as adhesion to plastic cell culture dishes, versatile differentiation and especially carrying certain phenotypic surface markers, thanks to surface markers from hematopoietic stem cells (CD105, CD54 (ICAM-1), CD49e. (α5-integrin), CD73 and CD39) and can be separated easily. The most striking feature of MSCs, especially in terms of regenerative medicine; It has the potential to transform into a wide variety of cell types, especially connective tissue, by providing appropriate microenvironmental conditions. Studies have shown that in vitro conditions with appropriate cellular growth factors, they can form hematopoietic stroma as well as adipogenic, osteogenic, myogenic and chondrogenic differentiation potentials. Today, studies on the application of MSCs in degenerative diseases such as tumors, trauma, osteoporosis and osteoarthritis related to the skeletal system are increasing rapidly. It is also considered appropriate to use MSCs in cartilage and bone damage, and in osteoarthritis resulting from trauma and old age.

4. Use of Adult Stem Cells in Therapeutic The most important disadvantage of MSCs in terms of clinical use is that they need to be replicated in vitro for a few weeks due to their very small

number. These naturally increase the cost as they require a high technological infrastructure, expert and technical personnel experience. At the same time, it is predicted that this situation may lead to changes in phenotypic, immunological and other biological properties with the effect of various chemical stimuli and factors as a result of subculture of cells in culture medium. Although it is very difficult to compare the data on tumorigenesis in studies, the fact that these cells can form tumors even in immunologically healthy animals is still questioned whether they can be used safely in clinical terms. Despite that; As a result of stem cell treatments in animal models of certain human diseases; The absence of a tumor is also an important finding that should be emphasized. Tissue engineers have shown that MSCs derived from bone marrow are promising in their experimental studies. However, isolation of very small amounts of MSC from the bone marrow biopsy method, which includes an invasive method that requires general or spinal anesthesia, and the possibility of cell contamination and cell loss limit its use. For these reasons, studies have increased on cells that do not disturb the comfort of the patient much, can differentiate into the desired tissue, and can be used for the maintenance and repair of tissues. Bone marrow-derived cells are a good example for adult stem cells. Bone marrow stem cells have been used in hematological diseases for

more than 40 years. Adult stem cells are cells that maintain their ability to regenerate themselves throughout the organism's life. Despite this, they cannot be produced outside the body by preserving their specific characteristics like embryonic stem cells for a long time. Adult cells differentiate into precursor cells and then into specific cells. In this respect, it is very difficult to isolate adult stem cells from tissue-specific precursor cells. It has been reported that stem cells originating from adipose tissue have the potential to differentiate as much as stem cells originating from bone marrow. When the bone marrow and adipose tissue are compared; more stem cells can be obtained from adipose tissue. In tissues and organs where adult stem cells are located; It was thought that these cells could only differentiate into a certain group of cells, but nowadays it has been reported that these cells can differentiate into kidney, bone marrow cells, skeletal muscle, nerve and liver cells. Besides; Today, it has been shown that an adult cell can differentiate into a pluripotent stem cell by undergoing a backward change with a number of transcription factors. In another study, stem cells derived from the tissue lining the nasal cavity have been shown to have a high differentiation ability like embryonic stem cells. The fact that adipose tissue is of embryonic mesoderm origin like bone marrow and contains heterogeneous stromal cell population has led to the idea that

MSCs can be obtained from adipose tissue. A stem cell population that has the ability to differentiate into more than one different tissue group has been isolated from adipose tissue. He proved that this cell population did not consist of different precursor cells, but was a single type of cell, and these cells said, ğ Tissue Originated Stem Cell (YDKKH); Adipose- derived stem cells (ADSCs). In addition to the differentiation of these cells into different mesodermal cell types such as adipogenic, chondrogenic, osteogenic and myogenic, effective proliferation abilities in cells with mesenchymal stem cell potential have also been demonstrated. Besides; Their differentiation into tissue groups of ectodermal origin (such as neurons, oligodendrocyte-like cells, functional Schwan cells) and their differentiation into some cells from the endodermal line such as hepatocytes and pancreatic islet cells were also performed. Today, stem cells are being studied with different biomaterials in tissue engineering. For example, post-ischemia revascularization, cardiovascular system regeneration, repair of bone-cartilage defects, intervertebral disc regeneration, spinal cord injuries and urinary system reconstruction are current studies. Isolation of adult adipose tissue stem cells has many advantages such as being less invasive and easy to obtain, obtaining more cells, and rapid adhesion and proliferation. In general, for MSCs originating from

adipose tissue, pre-study for many diseases in vitro and in vivo is applied to the cells of the 2nd, 3rd and 4th passage after isolation. Various surface markers are used to determine the phenotypic characterization of ADSCs at passage 3 and beyond. Characteristic adipose tissue surface markers for ADSCs, CD26, CD105, CD29, CD39, CD54, CD90, CD73, vimentin (C-20), fibronectin (EP5), ASMA, myogenin (F5D), MAP 2a,b (AP20) , Ki67, PCNA, and tenascin-C have positive immunohistochemical properties, while CD71 (K-20) cytokeratin, CD45, CD34, CD14, CD11b, CD79 alpha and CD19 are immune negative markers. These surface markers define whether the cells are stem cell or not. Today, clinical studies in which stem cells produced in-vitro are used as direct treatment agents are increasing rapidly. At the same time, the effects of various pharmacological or chemical agents on stem cells are the subjects of investigation for many diseases in the field of regenerative medicine. Especially muscle and nervous system heart diseases , autoimmune diseases , type 2 diabetes , multiple sclerosis, chron's, acute graft-versus-host , tendinitis (Regenerative applications are performed with MSCs for the treatment of degenerative diseases such as 36), arthritis, corneal degenerations, refunction of the glomerular-capillary wall , parkinson's.

Stem cells; It is a cell type defined by its ability to multiply unlimitedly, renew itself, differentiate into other cells, and repair the tissue when given to the damaged tissue. They are preferred in regenerative medicine applications because they are abundant, easily obtained, multiply by differentiation into many cell types, and can be safely and effectively transplanted to autologous or allogeneic recipients. Stem cells are called totipotent, pluripotent, multipotent, oligopotent and unipotent according to their differentiation capacity. Totipotent stem cells are cells that theoretically have the capacity to form an organism. The zygote is the first totipotent cell that has the potential to differentiate into all cell types that will form the organism. Totipotent cells can show pluripotent, multipotent and unipotent properties by forming the extra-embryonic umbilical cord, amniotic sac, Wharton gel and placenta. Pluripotent cells, on the other hand, have the capacity to form tissues of all germ leaves (endoderm, ectoderm, mesoderm). They can form fetal or adult cell types, but are not capable of forming an organism. The differentiation of multipotent stem cells is more limited. They are cells that can transform into only a few cell types in the human body. It is possible for them to transform into more cell types when the necessary conditions and signals are provided in the laboratory environment. Unipotent cells are cells that have the ability to

differentiate into a single group of cells in an advanced organism. They also play a role in tissue regeneration, but pluripotent stem cells are needed for the repair of extensive tissue damage (16, 17).

Self-Renewal Feature

Stem cells divide in order to ensure their continuity in tissues, and their division results in the formation of new stem cells. This event is called self-renewal of the stem cell. In these divisions, the stem cell undergoes asymmetric and symmetric divisions. While one of the resulting two cells has the same characteristics as the main stem cell, the other continues to divide and differentiates (18). Asymmetric cell division has an important place in cell fate in terms of maintaining the balance between self-renewal and differentiation of the cell. Asymmetric cell division occurs under the control of internal and external factors(19). Symmetrical division is necessary for tissue repair, tissue volume expansion, and to meet the need for new cells in the developmental process of the embryo. In this case, stem cells step in by transforming into progenitor cells. They are capable of multiple divisions (20). Stem cells that remain undifferentiated provide the continuity of stem cells in the tissue. The occurrence of a defect in the self-renewal mechanism may cause developmental delay and cancer in the organism. By

understanding the self-renewal mechanism in stem cells, the causes of cancer and aging can be explained.

Differentiation Capability to Different Cells (Potency) The concepts of pluripotency (multi-competence) or differentiation richness are used to describe the stem cell's capacity to differentiate into a specialized cell. Pluripotency is the most important feature that distinguishes stem cells from other cells. Stem cells form a hierarchy according to their potency properties. While some of the stem cells show the ability to differentiate only into a specific cell, some of them can form the whole organism (21).

Stem Cell – Progenitor Cell

Progenitor cells are cells that can differentiate to form one or more cell lines. These cells cannot divide and multiply indefinitely. The diversity of a progenitor cell is more limited than a stem cell. However, it has uses in medicine. These cells are the cells involved in the phase between stem cells and mature, functional cells.

Cloning Ability (Clonality)

Another basic feature of stem cells is their ability to form clones. The word 'clone' can be thought of as a collection of cells that are

similar to each other. The stem cell, which divides and creates its own clone, differs from other previous clones with its shape and physiological properties.

Stem Cells by Source

1) Embryonic Stem Cells: These cells are pluripotent in the inner cell mass of the embryo (4-5 days old) at the blastocyst stage, that is, the ability to transform into the three germ layers of the embryo (endoderm, mesoderm, ectoderm) and different cell types originating from these layers. competent cells. In order for embryonic stem cells, which have the capacity to divide without differentiation, to proliferate in vitro conditions, it is necessary to provide an appropriate culture medium.

Induced Pluripotent Stem Cells

Nobel Prize-winning research has shown that adult cells can be "reprogrammed" into cells that behave like embryonic stem cells, thanks to a revolutionary advance in stem cell research. Cells that are formed by the activation of some genes in the DNA of a normally non-pluripotent cell by external stimuli are called induced pluripotent stem cells. These cells are in many ways like a normal pluripotent stem cell (22). However, the use of these cells in cell therapy is currently theoretical. The technology is

very new and the reprogramming process is not yet fully understood. Scientists are looking for ways to produce these cells safely and efficiently.

Ethics in Embryonic Stem Cells

Embryonic stem cells have opened up hope for new treatments, but debate over their use in research continues. Ethical debates in research continue on the axis of the use of embryos, adult stem cell research ethics, the responsibility of scientists, the use of animals in experiments, and the approach of religions to the subject (23). Since embryonic stem cell research is handled differently between countries, regulations on this subject also vary. The National Institutes of Health (NIH), located in the United States, announced on April 27, 2010 that 13 additional stem cell lines, including the most widely used lines from human embryonic stem cells, are eligible for federal funding (24).

2) Non-Embryonic Stem Cells:

The capacity of non-embryonic stem cells is more limited. In addition to the ability of these cells to renew themselves in line with their needs, they also have the ability to differentiate into precursor and specialized cells found in adult tissues. Multipotent hematopoietic and mesenchymal stem cells, which are classified

as non-embryonic adult stem cells, are the most studied cells. Other unipotent adult stem cells are musculoskeletal system, cardiovascular system, nervous system, digestive system, epithelial tissue, testis and ovarian stem cells.

Stem Cells According to Division and Differentiation Characteristics

Totipotent Stem Cells: After fertilization, embryonic stem cells retain the ability to form the three germ layers as well as extra-embryonic tissues or placental cells and are called totipotent. Totipotent stem cells, which have the amount and characteristics of DNA that can form the whole organism, have the potential to form all cells, extra-embryonic membranes and placenta in humans. The fertilized egg (totipotent) forms the blastocyst, a 300-cell structure containing embryonic stem cells in its inner cell mass. Embryonic stem cells are pluripotent and therefore can differentiate into all cell types in our body, including adult stem cells ranging from multipotent to unipotent.

Pluripotent Stem Cells:

The stem cells of embryonic origin obtained from the inner cell mass of the embryo are called pluripotent stem cells. These cells, which form the inner cell mass of the blastocyst, can differentiate

into all cells in the organism. These more specialized cells in the blastocyst stage retain the ability to self-renew and separate into three germ layers. However, they do not form extra-embryonic tissues or placental cells (25).

Multipotent Stem Cells: These cells can only form certain cells. For example, multipotent stem cells from a mesodermal tissue such as blood can form blood cells, but cannot differentiate into different cells such as nerve cells (ectoderm) or liver cells (endoderm).

Unipotent Stem Cells: These cells are; It has the ability to form cells of a single cell type, but its self-renewal feature requires it to be classified as stem cells. An example is muscle stem cells.

Figure 1. Adipose tissue Stem cell therapy

1. Methods Based on Measuring Metabolic Activity

(MTT, MTS, XTT, WST-1) 3-4,5-dimethyl-thiazolyl-2,5-diphenyltetrazolium bromide (MTT) test is a method generally used to measure cell viability. It quickly measures the activity of dehydrogenases primarily found in mitochondria. It is based on the fact that proliferating cells form formazan products with tetrazolium, and the color change that occurs is evaluated by absorbance measurement. When cell viability is lost, mitochondrial function and, consequently, its ability to convert tetrazolium salt to formazan are reduced. In many cells, the amount of formazan changes in proportion to the number of cells, and cell viability is determined by this amount change (26). If we want to compare tetrazolium species, the best alternative seems to be 2-(4-iodophenyl)-3-(4-nitrophenyl)-5-(2,4-disulphophenyl)-2H-tetrazolium, monosodium salt (WST-1), compared to other salts. it is consumed more efficiently and shows a faster color change. In the use of 2,3-bis[2-methoxy-4-nitro-5-sulphophenyl]-2H-tetrazolium-5-carboxanilide (XTT), it should be kept in mind that XTT is reduced slowly by cells and extra factors may need to be added. Since MTT is insoluble in the culture medium, additional solvents such as dimethyl sulfoxide (DMSO) are required to dissolve the reduction products (26).

1.1 Role of Stem Cells in Cytotoxicity Methods Based on Measurement of Metabolic Activity In a study using the MTT test, one of the formazan-based tests, dose-dependent cytotoxicity and genotoxicity of graphene oxide in mouse spermatogonial stem cells were investigated for the first time. According to the MTT results, the cell number decreased in samples treated with high concentration (100 and 400 µg/ml) graphene oxide compared to untreated cells. As a result of the study, it was noted that high concentration graphene may be toxic to spermatogonial stem cells, but this toxicity can be reduced by surface modification of graphene nanomaterials. The current study states that spermatogonial stem cells, which are responsible for producing germ cells that transmit genetic material to offspring, are very sensitive to toxic substances such as nanoparticles. However, it is known that graphene nanomaterials are increasingly used in biomedicine and industry. In another study evaluating cell viability with MTT, magnesium-based alloys used in biodegradable implant materials in orthopedic surgery were studied.

In this study, the cytotoxicity of biodegradable Mg-Zn-Ca alloys in adipose-derived mesenchymal stem cells was evaluated. At the end of the study, Mg-Zn2-Ca alloy was recommended as a good

candidate to be used in biomedical devices (27). Burnett et al. showed that sulforaphane increases the anticancer activity of taxanes against triple negative breast cancer by killing cancer stem cells. Sulforaphane is an isothiocyanate primarily derived from cruciferous vegetables and has been extensively studied as a cancer prevention agent. Recently, sulforaphane has been shown to destroy cancer stem cells in several types of cancer. In this study, cell viability was evaluated by MTS method and studied with breast cancer stem cells. It was concluded that sulforaphane inhibits cell proliferation of taxane-induced aldehyde dehydrogenase. The combination of docetaxel and sulforaphane has been shown to significantly reduce tumor formation, and sulforaphane has been shown to be beneficial in preventing and eliminating the spread of breast cancer (28). The cytotoxicity of various nanocarbon nanotubes in mesenchymal stem cells obtained from rat bone marrow was evaluated using the WST-1 test. Carbon nanotubes are modified with polymeric surfactant because they cause cytotoxic effects on mesenchymal stem cells in biological environments. In this research, various pluoronic F-68 coated multi-walled carbon nanotubes were studied. There was no change in cell viability after 24 hours, but it has been reported that toxicity may increase as the exposure is prolonged (reaches 48-72 hours). This study proposes that the

appropriate polymer coating can reduce the acute toxicity of multi-walled carbon nanotubes without altering the biological fate of stem cells (29).

2. Membrane Permeability Tests

Cell membrane permeability can be easily determined by means of a membrane-penetrating dye. One of the foundations of this method is that the cell membrane permeability of the cell, which is close to extinction, has increased. Living and dead cells are determined according to whether the dye can pass through the cell membrane. Vital dyes, one of the two types of dyes used in this method, are transported to the living cell by active transport. Neutral red is an example of the most commonly used vital dye. Trypan blue, which is one of the non-vital dyes, enters the cell when cell viability ends (30).

2.1 Neutral Red Test

The principle of the neutral red method is based on the accumulation of neutral red dye in the lysosomes of living and healthy cells. This method is fast and colorimetric. In cases where the integrity of the cell is disrupted, if the cell membrane or the more sensitive lysosome membrane is damaged, the neutral red dye cannot enter the cell and bind, and thus a colorometric

decrease is experienced. In this way, it is possible to distinguish between living healthy cells and damaged dead cells (31).

2.1.1 In Neutral Red Test

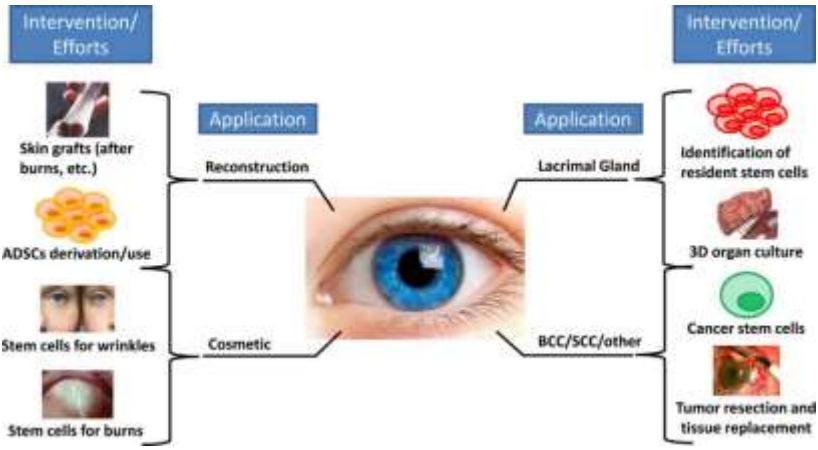
The Role of the Stem Cell In a study investigating the cytotoxic and genotoxic effects of arsenic and lead in human adipose-derived mesenchymal stem cells, the cytotoxic effect was evaluated by the neutral red method and the genotoxic effect was evaluated by the comet method. At the end of the study, the growth of cells decreased with increasing arsenic concentration and exposure time. The current study shows that both arsenic and lead have cytotoxic and genotoxic effects on these stem cells, but arsenic has been reported to have more harmful effects compared to lead.

2.2 Trypan Blue Method

Trypan blue is negatively charged. If the cell membrane is intact and a living cell, the dye will not enter the cell. However, non-viable cells absorb the dye and appear blue under the microscope. A point to note when working with trypan blue is that viable cells are also stained blue if the cells remain in the trypan blue dye for longer than the specified time (32).

Stem cell is an unspecialized mother cell type that can reproduce by mitosis and can both renew itself and differentiate into other specialized cell types (33). The existence of stem cells in the bone marrow was first described by Freindstein in 1976. In the historical process, its first use was in experimental studies to alleviate the effects of radiation on the bone marrow. Their existence was first demonstrated by Zuc in 2001 (34). While there are approximately 5000 colony-forming units (CFU) in 1 gram of adipose tissue, 100-1000 CFUs are present in 1 ml of bone marrow-derived material. After proving the efficacy of adipose tissue-derived stem cells (ADCSC) in in-vivo and in-vitro studies, in addition to plastic surgery in the field of regenerative medicine and tissue engineering, NSBC can provide other stem cells such as neurology, urology, orthopedics, and physical therapy (35). However, there are still unclear issues regarding the mechanism of action of YDKKH, its location, proliferation and differentiation characteristics in the area where it is applied, and its clinical use. Standardization has not yet been achieved in clinical use and optimization studies are still in progress, due to the body area from which the YDLCC is obtained, the technique applied during its preparation, and the type of stem cell materials to be used (cultured stem cell or stromal vascular fraction-SVF) (36). The aim of this study is to The aim is to share basic

information with YDKKH, to review its mechanisms of action in the light of literature, and to attract plastic surgeons' attention to its uses in plastic surgery.



Figre 2. Overview of primary oculoplastic areas benefiting from stem cell intervention and examples of stem cell efforts currently being made in these areas (37).

Stem cells are present in the human body from the formation of the zygote. In the third day embryo, which consists of only eight cells, all cells are called totipotent embryonic stem cells. Totipotent stem cells have the potential to transform into placenta and whole body cells. With the continuation of cell division. Within days, pluripotent embryonic stem cells develop from the

blastocyst inner cell mass, which can transform into ectoderm, mesodem, and endoderm cells that form different tissues of the body. However, Yamanaka et al. showed that adult, differentiated, and specialized somatic cells can transform into pluripotent stem cells by induction of appropriate transcription factors (OCT3/4, Sox2, c-Myc, and Klf4).28,29 Adult stem cells are stem cells derived from post-embryonic tissues. These cells are non-specialized cells that can proliferate in cultures without differentiation for a long time (for 37 passages), but have the potential to become specialized.12 Adult stem cells are basically divided into three main categories: 1. Hematopoietic stem cells that make up blood cells, 2. Osteoblasts, chondroblasts, adipocytes. Mesenchymal stem cells from which it originates, 3. Organ-specific, unipotent stem cells. The criteria defined by the international cell therapy community for stem cells of mesenchymal origin can be listed as follows; 1. Adhesion to plastic and glass surfaces, 2. Minimum expression of CD73, CD90, CD105 on the cell surface, as well as the negativity of hematopoietic stem cell markers CD45, CD34, CD14 or CD11b, CD79 alpha or CD19 and HLA-DR surface molecules, 3. It has the ability to transform into mesenchymal cells such as adipocytes, chondrocytes or osteoblasts in-vitro. 30 In-vivo and in-vitro studies have shown that these cells can also transform into

cells of endoderm and ectoderm origin, in addition to mesoderm, in the future (38).

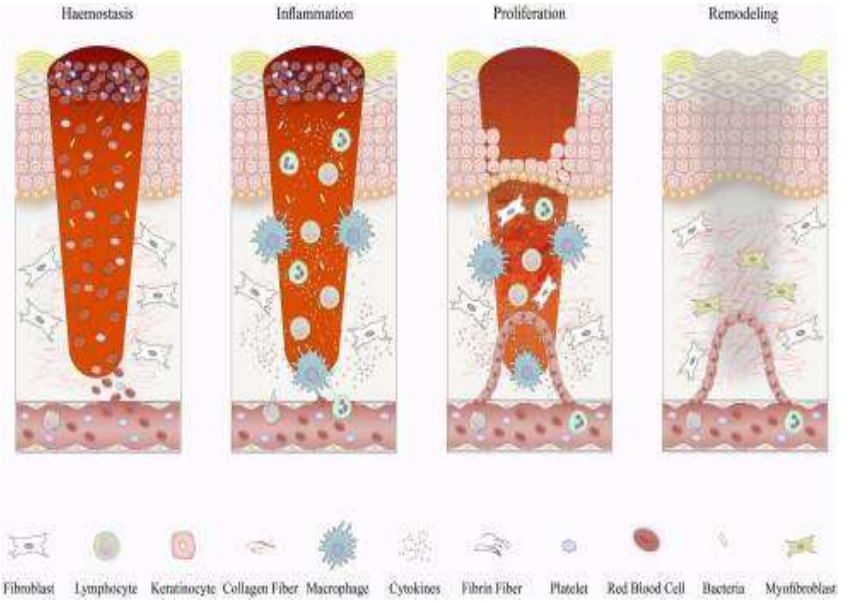


Figure 3. Schematic representation of the phase involved in in vivo wound healing and the cells that respond to them (37).

Exosome consists of lipid bilayer with small cytosol without cellular organelles. After secretion, exosomes act as messengers and thus facilitate interfaces with recipient cells through the vesicular docking and fusion procedure. This event is facilitated by soluble N-ethylmaleimide sensitive factor binding protein receptor (SNAREs) complexes as well as the endosomal sorting

complex (ESCRT) required for transport. However, MVB biogenesis can be completed without ESCRTs, as demonstrated by the generation of intraluminal vesicles (ILVs) without the involvement of ESCRT complexes.

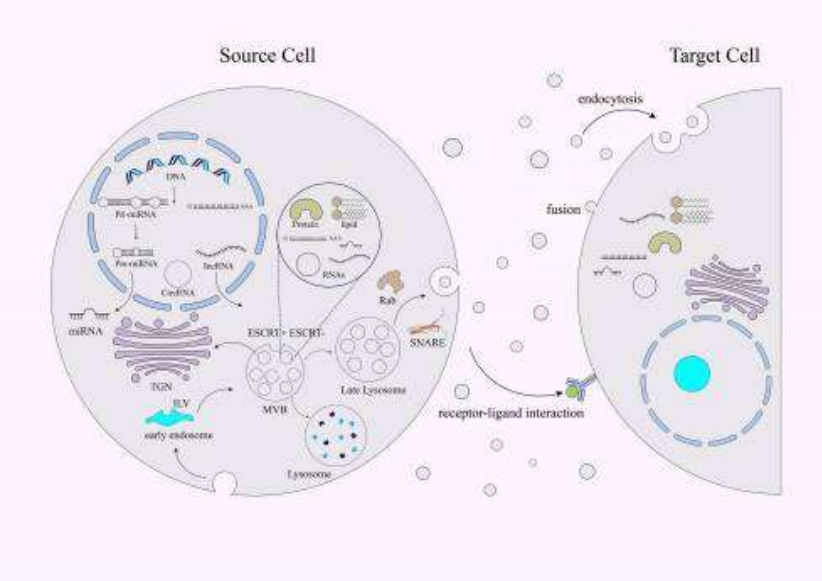


Figure 4. Schematic representation of the biogenesis of the exosome, its compositions as well as its release. Following MVB fusion with the cell membrane, the exosome is released into the extracellular space and finally the released molecules are transported to the recipient cells via endocytosis or direct membrane fusion or receptor-ligand interfaces. Intraluminal vesicles (ILVs), Endosomal complexes required for transport

(ESCRT), Multivesicular bodies (MVBs), Trans-Golgi network (TGN), Ras-related in brain (Rab), Soluble NSF supplemental protein receptor (SNARE) (37).

MSCs can intensely target immune responses throughout tissue repair and offer a favorable soil for tissue repair and regeneration (39). In addition to direct cell-to-cell contact of MSC, the complex mechanisms in such immunomodulatory effects are likely related to the capacity of MSCs to secrete various soluble factors that influence the biological process of the target cell (40). In fact, MSCs alter adaptive and innate immunological reactions by abolition of T cell activities, inhibition of dendritic cells (DCs) maturation, reduction of B cell activation and proliferation, and finally the activation of NK cells and ultimately the cytolytic effect on the target. cells. Of course, T regulatory (Treg) cell proliferation and function inspired by paracrine action or cell-cell contact mechanisms maintain MSC-mediated immunoregulation (41). Paracrine action as shown, transforming growth factor-β1 (TGF-β1), prostaglandin E2 (PGE2), indoleamine-pyrrole 2, 3-dioxygenase (IDO), hepatocyte growth factor (HGF), nitric oxide (NO), and interleukin (IL) -4) and IL-10 (42). In damaged tissue, the presence of proinflammatory cytokines such as IFN-γ, tumor necrosis factor-α (TNF-α), IL-1α or IL-1β can cause activation of

MSCs and subsequently promote their release. Various enzymes and soluble factors, including IDO, PGE2 and cyclooxygenase 2 (COX-2). Such mediators potentiate the immunosuppressive functions mediated by MSCs. Meanwhile, PGE2 inhibits T-cell proliferation and IDO influences the expansion as well as activation of immune cells by catalyzing the breakdown of tryptophan, which is essential for T-cell effector functions. Furthermore, NO produced by MSCs can inhibit immune cell growth by suppressing the signal transducer and activator of transcription 5 (STAT5) phosphorylation, and also through interfaces with various enzymes, ion channels, as well as receptors (43). Considering that suppression of inducible NO synthase (iNOS) production in MSCs mainly leads to enhanced T-cell activity, NO appears to play a pivotal role in MSC-mediated immunoregulation. Moreover, treatment of MSCs may improve bacterial clearance through increased migration. It facilitates and enhances the phagocytic functions of neutrophils by increasing the levels of IL-6, IL-8 and granulocyte-macrophage colony stimulating factor (GM-CSF). These molecules promote removal of infection and facilitate tissue repair, as shown in wound healing.

Identification of Adipose Tissue Stem Cells

Although 90% of the cells that make up the adipose tissue are adipocyte, as a result of the examinations made by flow-cytometry, in the adipose tissue; mature adipocyte, preadipocyte, post-adipocyte (cells that transform into fat cells during obesity and remain as adipocyte instead of fibroblast, which is the old cell type, again with weight loss), mesenchymal stem cell, macrophage, fibroblast, reticulocyte, vascular endothelial cells, mast cells and nervous system (44). Yoshimura et al. reported that intact adipose tissue consists of 16% adipocytes, 30% adipose-derived stem cells, 15% endothelial cells, 9% blood-derived cells, and 30% other cells. Stem cells are adipose tissue. Although there are interpretations that there are pericytes around blood vessels within the blood vessels or that there may be a subpopulation of fibroblasts, their origin has not yet been clearly defined. Recently, it is derived from other adipose-derived stem cells, which are defined as SSEA-3 (Stage specific embryonic antigen) among adipocytes in adipose tissue. different new types of multipotent master cells have been discovered. This information is important in terms of revealing the existence of multipotent stem cells, one localized in the adipose tissue and activated only in emergencies, and the existence of progenitor cells located around the capillaries

and regulating the physiological transformation of the tissue. Adipose tissue-derived stem cells are differentiated from other endothelial cells, macrophages and peripheral monocytes by the presence of different but stable surface reagents, with a minimum of CD105, CD73 and CD90 (45).

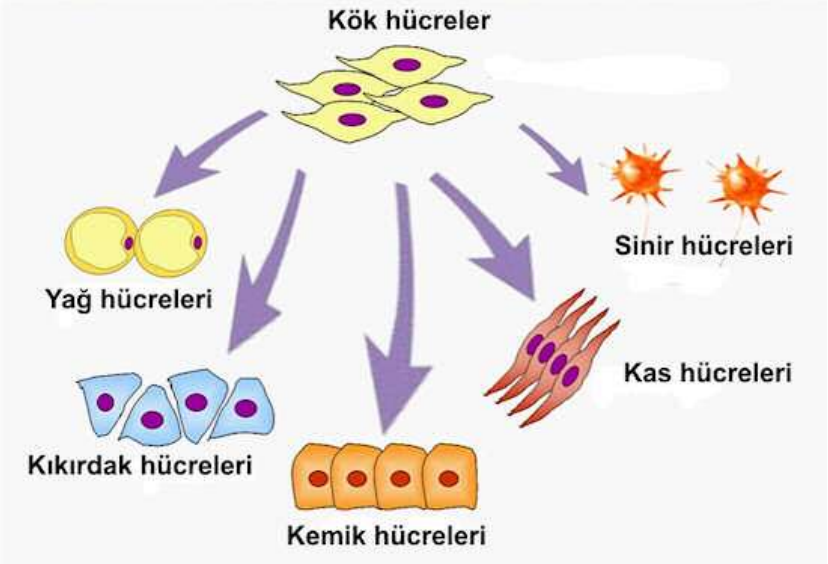


Figure 5. Stem cell

Direct implementation of MSCs

Human MSCs are known to proliferate extensively and differentiate into skin cells to regenerate injured or dead cells, but also work through an autocrine and paracrine pathway to stimulate cell regeneration and wound healing. MSCs can migrate

to injured sites and differentiate into dermal fibroblasts (DF), endothelial cells, and keratinocytes. Furthermore, MSCs and DFs can produce complex extracellular matrix (ECM) proteins in supporting skin structure and activity. In summary, MSCs modify the inflammatory phenotype of the macrophage which contributes to the inflammatory phase, enhance the formation of new blood vessels, lead to promoting angiogenesis and finally facilitate the production of granulation tissues, skin cells and ECM (46).

In vivo studies have shown that allogeneic BM-MSC treatment causes significant changes in the wound repair kinetics of lesions in the excisional wound splinting mouse model. Murine treated with allogeneic MSCs experienced improved wound closure and accelerated granulation tissue formation with less inflammatory response. Such desirable events are most likely caused by MSCs, including IGF-1, VEGF, MMP-1, keratinocyte growth factor (KGF), HGF, angiopoietin-2 (ANG-2), type 1 collagen (COL1), and PGE2. secreted molecules cause. BM-MSCs, but not CD34+ BM cells in the wound, showed keratinocyte-specific protein keratin and shaped glandular structures ;]. Wu et al. also showed that MSCs can produce high levels of VEGF and angiopoietin-1; this indicates that stem cells improve wound healing through

differentiation as well as secretion of molecules that induce angiogenesis.

How metazoans form and maintain organ size is a fundamental question in developmental biology. While organ size is largely determined during development and adolescence in mammals, there is limited size change after adulthood (47). However, in adult mammals, the skin has a remarkable capacity for growth dynamics. Significant growth of skin occurs in response to the increase in body mass, but once created, new skin is not easily lost. This may be problematic, as in patients with excessively saggy skin after postbariatric weight loss (48). In contrast, in pregnant women, the new skin on the abdomen and chest that forms to meet the demands of fetal growth and breastfeeding regresses significantly after birth. Adult skin growth capacity is also used therapeutically in a process known as tissue expansion. To replace skin lost due to surgical resection or trauma, surgeons place silicone balloons, known as tissue expanders, under the skin and gradually increase their size with saline injection. Much like a growing fetus triggers skin growth, the slow process of tissue expansion leads to the formation of new skin that can be used to reclose wounds. The cellular and molecular mechanisms that support skin growth in these various conditions are of great

interest, especially since skin size is remarkably constant despite constant variation under homeostatic conditions. Understanding these mechanisms is a prerequisite for designing treatments for excessive or insufficient skin conditions and may provide broader insights into size control and induced regeneration in other adult organs. During epidermal maintenance, stem cells of the interfollicular epidermis (IFE) undergo divisions that give rise to additional stem cells and processed keratinocyte precursors. Elegant in vivo imaging studies suggest that delamination and subsequent differentiation of basal layer precursors from the basement membrane may stimulate keratinocyte stem cell division during homeostatic regeneration (49). A related stem cell mobilization and differentiation program underlies HF regeneration in the anagen, catagen, and telogen cycles. It is unknown how these homeostatic processes are disrupted to form new skin in response to growth stimuli such as pregnancy or tissue expansion. A few mechanical questions arise. First, what morphological changes occur in the epidermis, dermis, dermal appendages, and subcutaneous tissues during stimulated skin growth? It is unknown whether these subcomponents of the skin grow in harmony or respond differently to growth stimuli. Second, which cells are activated to form new skin, and what signals drive this growth? In homeostatic conditions, skin stem

cells are limited in their spatial localization and differentiation potential, but they may exhibit lineage disloyalty in conditions such as wound healing (50). Identifying source cells for newly formed skin is a critical explanatory step and will shape efforts to use this phenomenon therapeutically. Finally, how to restore homeostasis after skin growth is complete? When growth stimuli such as tissue expansion are stopped, are growth pathways passively interrupted or are there active brakes that delay further growth?

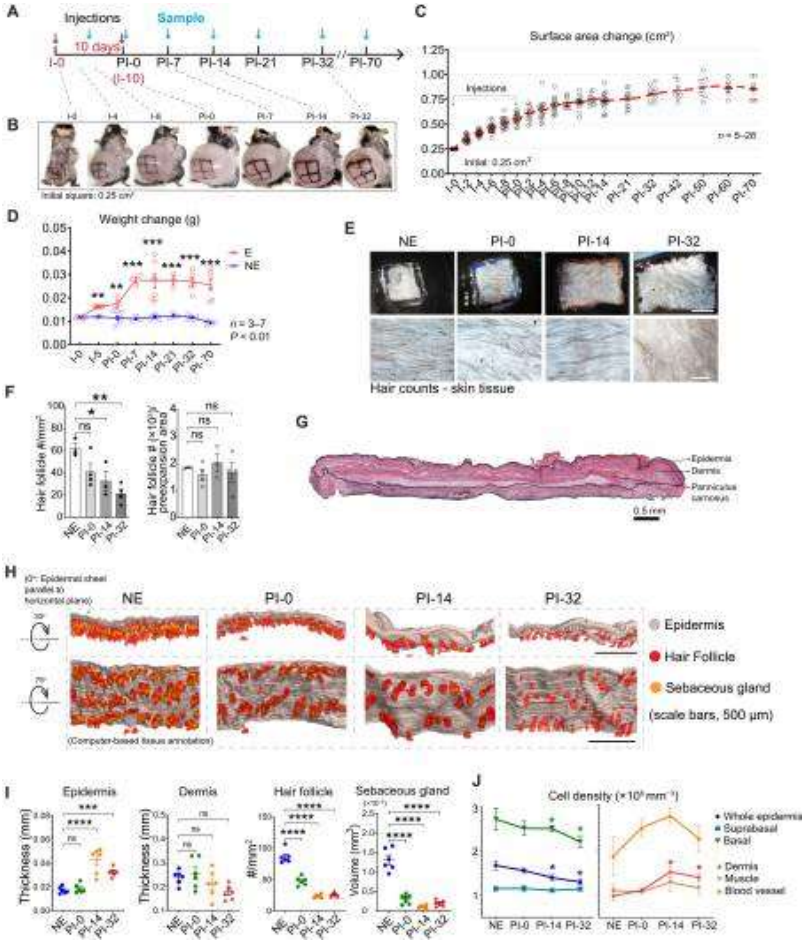


Figure 6. Morphological changes in the skin during tension-mediated growth (51).

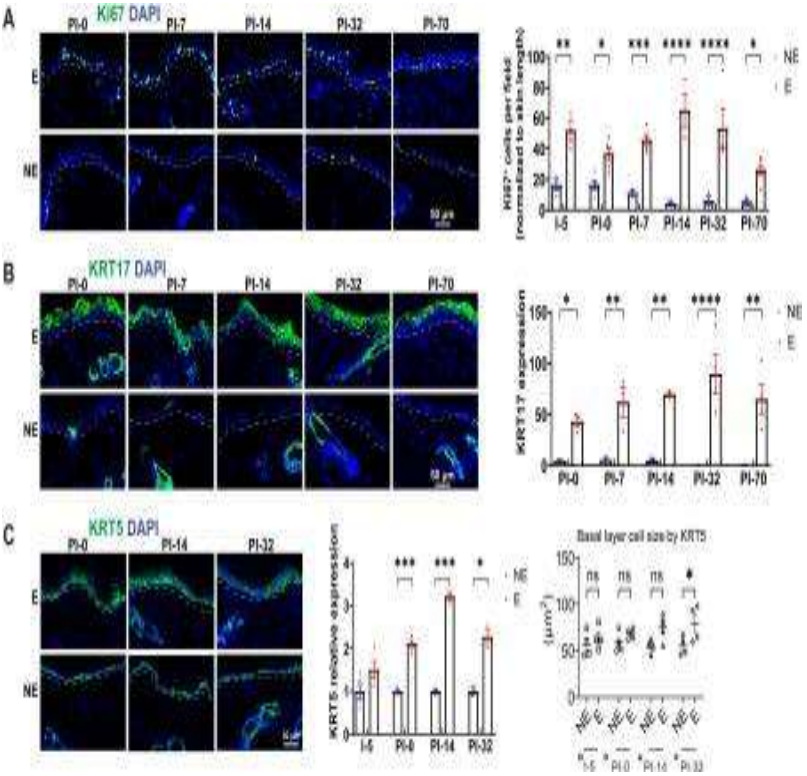


Figure 7. Mechanical tension stimulates proliferation and stem cell activation in the epidermis (51).

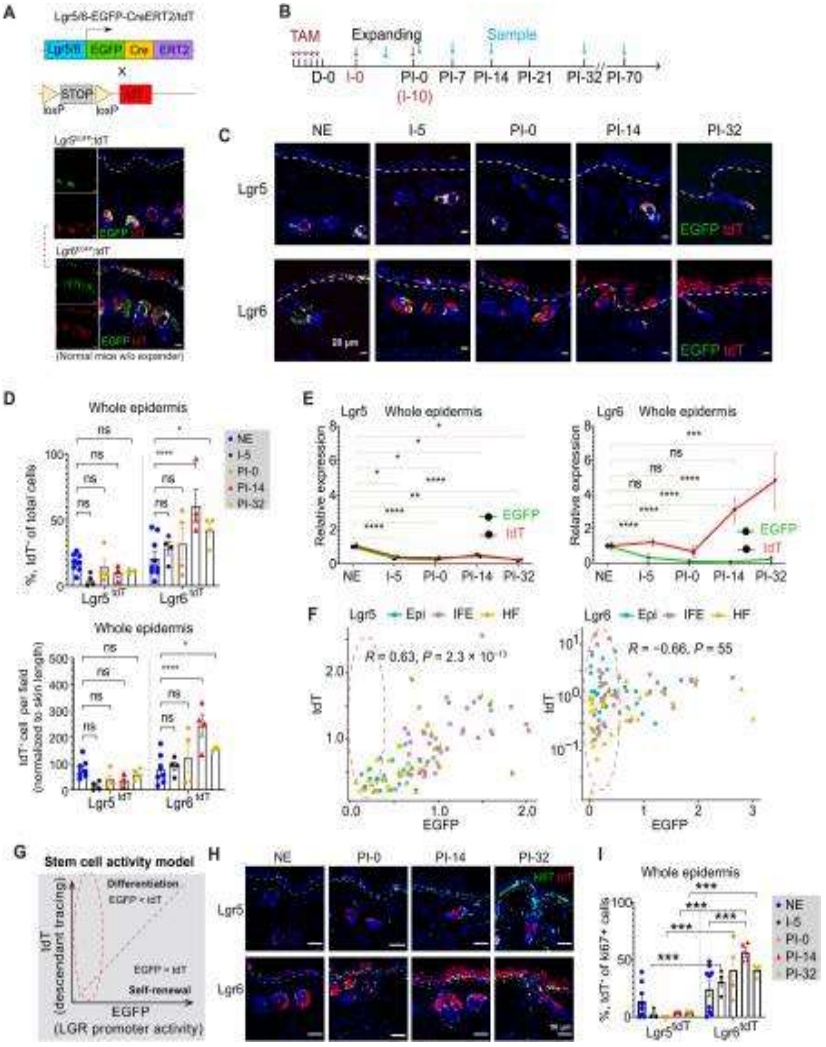


Figure 8. Tension enables preferential differentiation of Lgr6+ stem cells during skin growth (51).

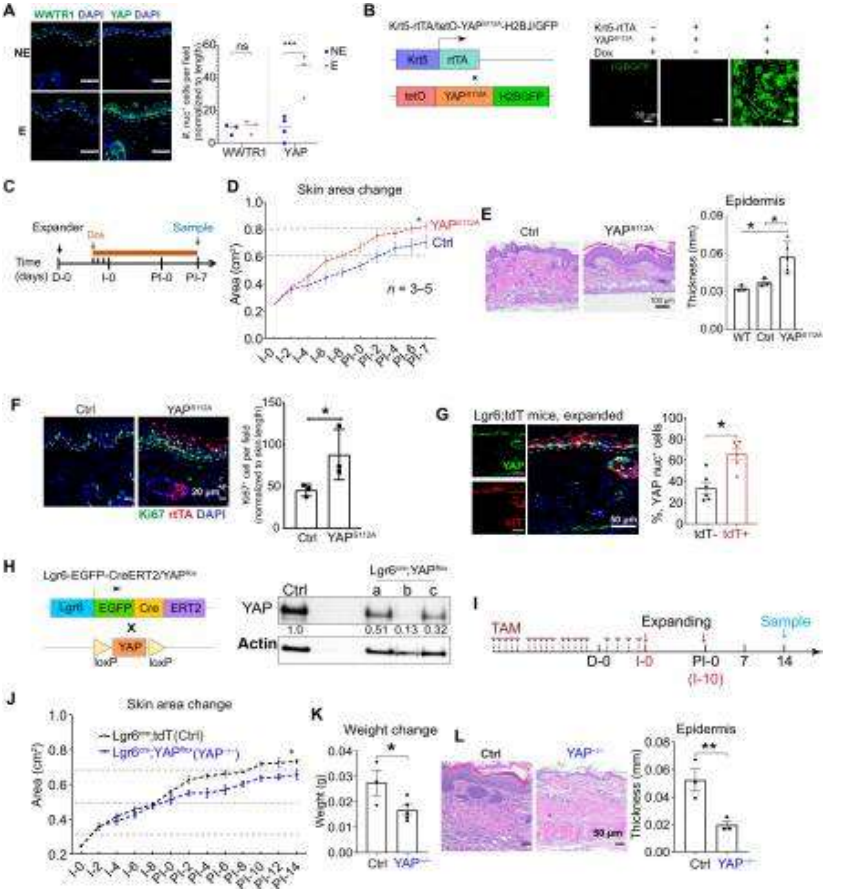


Figure 9. YAP mediates skin growth during tissue expansion (51).

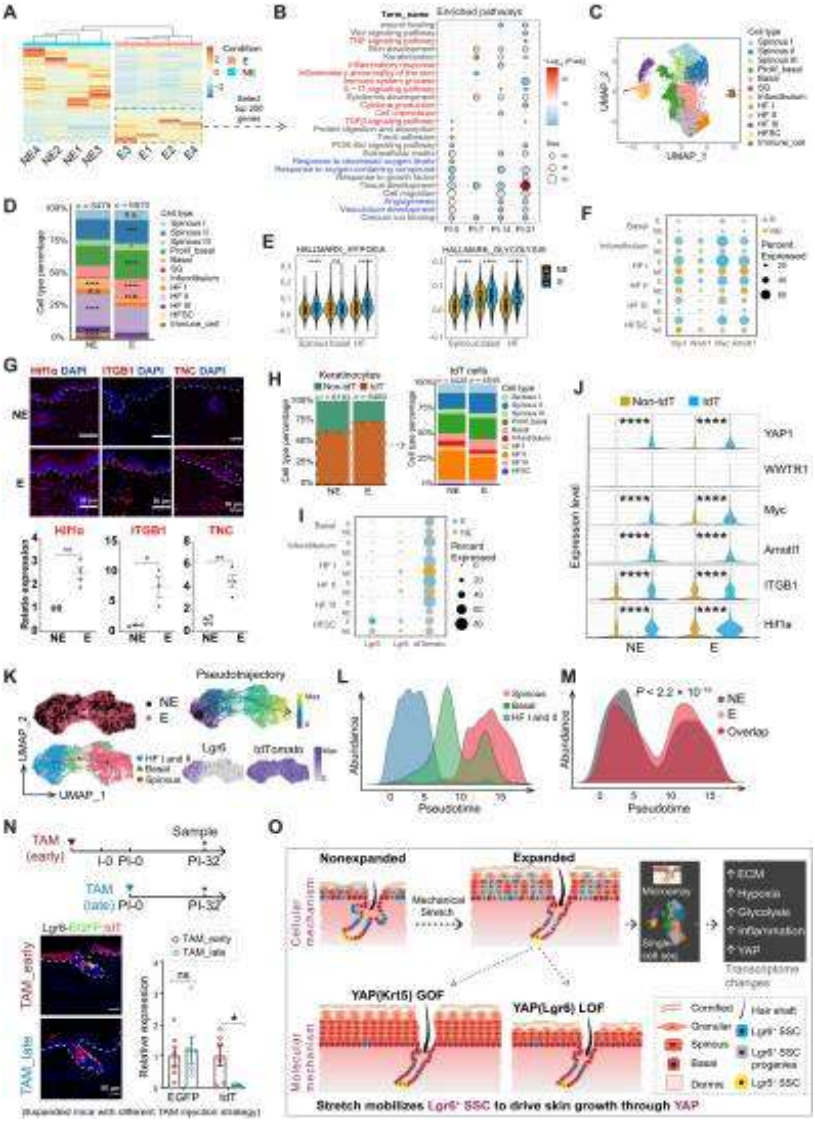


Figure 10. Cellular and transcriptomic changes during tension-induced skin growth (51).

Effect Mechanisms of Adipose Tissue-Derived Stem Cells in Tissue Repair

Contribution of stem cells to tissue repair occurs especially in the presence of tissue injury. Stem cells, which are normally silent in healthy tissue, migrate from the surrounding tissues and bone marrow to the injured tissue as a result of endocrine and paracrine calls (with selectin, chemokine, integrin interactions) that occur after injury. In addition to stimulating differentiation and differentiation, they also exert anti-inflammatory and immunomodulatory effects through the growth factors and mediators they secrete, and contribute to the remodeling of the matrix. illustrated by the reaction. However, the debate on whether they basically make their effects by transforming into media cells or with paracrine functions is still ongoing (52). On the first day of tissue damage, the media can be transferred from injured tissues and activated platelets; basic fibroblast growth factor (basic fibroblast growth factor, bFGF), platelet-derived growth factor (platelet-derived growth factor, PDGF), epidermal growth factor (epidermal growth factor, EGF), transforming growth factor-β (transfroming growth factor-β, TGF- β) and tumor necrosis factor α (tumor necrosis factor α, TNFα) are released. Yoshimura et al., in their experimental study on

ischemia and reperfusion injury in adipose tissue; In response to the bFGF factor released into the environment on the 1st day of injury and in response to ischemia, it was determined that NSSCs not only proliferate, but also secrete hepatocyte growth factor (HGF), which is a strong vascular stimulant and fibrogenesis inhibitor (53). EGF released from apoptotic endothelial cells in the environment (54). In addition, stem cells reduce the release of pro-inflammatory cytokines (interleukin-1β (IL1β), TNF-α, interferon-γ and nitric oxide synthase (nitric oxide synthase) released from leukocytes infiltrating the injured environment), and anti-inflammatory cytokines (IL- It has also been observed that it increases the secretion of 1beta, IL-10, bFGF, TGF-β and the antiptotic gene Bcl-2). Of these mediators, especially TGF-β plays an important role in the management of the effects of mesenchymal stem cells on tissue damage and is located in a silent position in the surrounding adipose tissue. or other stem cells originating from the bone marrow by activating the environment. 2-4 of the injury. During the (inflammatory phase) days, mast cells and platelets located in the adipose tissue contribute to healing by secreting TNF alpha, VEGF, PDGF, TGF-B like other cells (55). 5-7 of the injury. It has been shown that VEGF, HGF, IL-8 and matrix metalloproteinase-8 (MMP-8) increase in the wound fluid during the proliferative days

(proliferation phase). In this way, while a group of cells due to ischemia go to apoptosis, on the other hand, a new generation of adipocytes is formed and the remodeling process is entered, and the injured adipose tissue is healed in about 2 weeks. 80 The number of stem cells in the environment and the matrix components that make up the microenvironment in which the stem cells are located determine whether the process will result in regeneration of new tissue or fibrosis and calcification. Another feature of stem cells is that they do not express human leukocyte antigens (HLA-DR) and can suppress allogeneic, activated lymphocytes (Treg). The immunomodulatory properties of LSCHD have been demonstrated in in-vivo and in-vitro studies.

Obtaining and Using Stem Cells of Adipose Tissue Origin

Stem cells derived from adipose tissue are obtained directly after excision and fragmentation of adipose tissue or by centrifugation of lipoaspirate materials after enzymatic fragmentation with collagenase and cultured and multiplied (56) In the experimental study of Ullman et al., fat obtained from the abdomen, thigh, waist and knee regions. No statistical difference was found between the viability rates when the tissues were compared in terms of the area to which they were transferred. In another study, it was determined that NSLCs located in the superficial part of

the abdomen (scarpa fascia) are more resistant to apoptosis than stem cells located in other anatomical regions (57).

Later, another study supported this observation. ha has been published.For experimental uses, the culture methods of stem cells have been standardized. The fat tissue that is fragmented or contained in lipoaspirate is washed with phosphated saline (PBS-Phosphate Buffered Saline) until it is cleared of all blood and excess fluids. Then, this adipose tissue is kept in a magnetic stirrer at 37ºC for 1 hour, and then it is allowed to enzymatically decompose with the addition of Type A collagenase, DMEM (Dulbecco's Modified Eagle Medium), fetal cow serum (Bovine Fetal Serum), streptomycin and penicillin. The material is centrifuged by hand and the upper part is discarded. The cell collection at the bottom of the centrifuge tube is known as the stromal vascular fraction and contains erythrocytes, fibroblasts, pericytes, endothelial cells, macrophages, and stem cells derived from adipose tissue (58). This cell cluster is transferred to culture dishes and 5 at 37ºC It is incubated with % CO2. The liquids in the culture containers are changed daily, and unlike other cells, stem cells adhere to plastic culture materials, so their isolation and proliferation is ensured within a few days. they are made ready. When it is desired to be used for tissue engineering purposes,

insulin, dexamethasone and indomethacin are added to the culture medium in order to increase the adipogenic differentiation potential of NSSCs, while the idea is that it results from a lack of ace to increase their osteogenic potential. With this application, it is aimed to increase the number of stem cells in the aspirated adipose tissue material. Because it is thought that a large part of the stem cells remain around the blood vessels in the donor area and do not come to the lipoaspirate, while the other part remains in the liquid portion of the lipoaspirate.

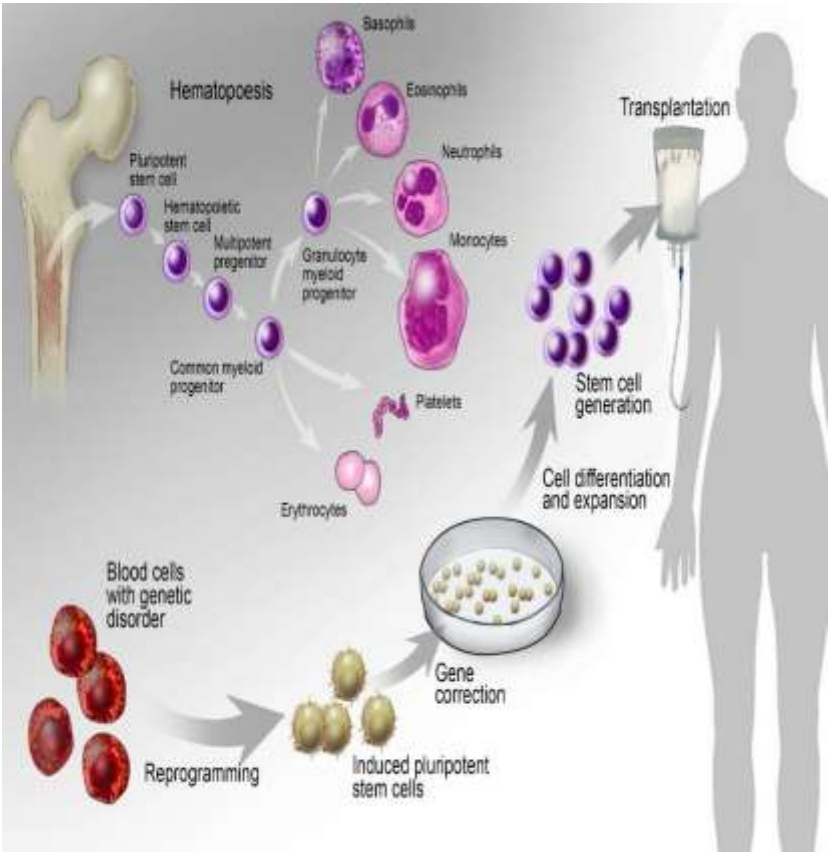
Use of Adipose Tissue-Derived Stem Cells in Plastic Surgery

YDKKHs continue to proliferate in the area to which they are transferred, and since they have the capacity of multipotent specialization, they respond to the need by manipulating them in accordance with the requirements of the area in which they are applied. In plastic surgery, NSCSCs are often used as a stromal vascular fraction or as isolated but uncultured cells. It has been reported that the age of the individual from which the stem cells were obtained has no effect on the viability and adipogenic potential of NSCLC (59).

a.Soft Tissue Volumization

Autologous adipose tissue transplantation is a technique frequently used for reconstructive and aesthetic purposes in plastic surgery, and breast reconstruction with adipose tissue transfer has gained popularity recently. However, due to the 40-70% atrophy of the transplanted adipose tissue and the uncertainty of the outcome, repetitive sessions are needed (60). The need for NSCLCs arises at this point. Since mature stem cells are not durable and especially sensitive to hypoxia compared to NSSCs, mature adipose tissue is enriched with stem cells.106 In clinical studies by Yoshimura et al. (61). Tiryaki et al. reported that lipoaspirate-enriched fat grafting yielded more successful results in secondary cases where fat grafting was applied but did not show adequate improvement (62). Kim et al. applied to depressed scarred areas and observed the transformation of cells into mature adipocytes in these areas (63). However, most of the published studies were studies without a control group, and there is still uncertainty about the clinical potential of NSCLCs.111 b. Wound Healing The most remarkable study investigating the effects of NSCLCs on wound healing was published by Rigotti in 2007. Following application of centrifuged and purified adipose tissue to radiotherapy-damaged tissues in repeated sessions after

liposuction, the healing of radiation-damaged tissue was attributed to stem cells in lipoaspirate. Lendeckel et al. LSCCHs were applied together with cancellous bone grafts in a patient with a large traumatic calvarial defect, and prominent ossification was detected in the tomographic examination taken at the 3rd month postoperatively. In 2009, Mesimaki et al. granules were prefabricated in titanium mesh and then the tissue obtained was transplanted into the maxilla as a microvascular flap. Bone remodeling was found in tissue biopsies (64). Recently, NSSCs have been diagnosed with neovascular iza- tion There are publications showing that it positively affects the viability of random pattern flaps by increasing the angle.



Figre 11. Stem cell production and use

Self-renewing stem cells, which form the origin of all structures in the human body, are used in the treatment of many diseases. It is a treatment method used to regenerate the damaged cells, tissues and organs of the patient by transplanting stem cells from the person himself, from a compatible or semi-compatible donor.

Previously, stem cell therapy can only be applied with stem cells taken from the bone marrow, but today it can also be taken from the peripheral blood and cord blood in the body circulation. In addition, recently, stem cells can be obtained from eggs (embryonic stem cells) and adipose tissue. In addition to heart, brain and nerve diseases, bone marrow treatment is generally a method used in the cases listed below.

• Correcting abnormalities caused by innate metabolism or enzymatic system

• Healing diseased or damaged bone marrow

• Elimination of suppression in the immune system

• Healing of damaged tissues and organs

As a result of scientific research, important developments have been made in stem cell therapy for the treatment of progressive diseases such as Alzheimer's and Parkinson's, as well as many neurological diseases such as stroke due to spinal cord injuries and cerebral vascular occlusion. When the stem cell is given into the brain tissue, although it is not effective in healing the damaged areas in the brain in some recent diseases and injuries, it has been seen that it provides healing in a different way by activating the cells on the healthy brain tissue. Thanks to many such newly

discovered properties of stem cells, stem cell therapy can be applied to cure many diseases in the near future. Stem cell therapy studies, in which research continues to cure many different diseases, continue at full speed. Therefore, the content of the answers to the questions of what is stem cell therapy and in which diseases stem cell therapy is effective is increasing day by day.

How is stem cell therapy done?

Today, stem cells are commonly used from peripheral blood, bone marrow and cord blood. Autologous transplantation is the transfer of the stem cell taken from the person to the damaged area in himself; Transplantation of stem cells from other donors to the patient is called allogeneic transplantation. In some cases, there is a treatment method defined as haploidentic transplantation, which is applied with stem cells taken from a semi-matched donor when the stem cell cannot be obtained from the person himself and a suitable donor cannot be found. After finding the appropriate stem cell, it is injected into the patient's vascular access or directly on the damaged area. The success rate of the treatment varies according to the type of the disease, the period and the complications experienced. In addition, in some cases, stem cell adhesion may not occur. In this case, the stem cell transplant needs to be repeated.

Reliability of Stem Cell Treatments

There are intense doubts about the effects of mesenchymal stem cells on cancer cells. In addition to publications suggesting that NSCLCs may activate cancer development in reconstructions performed after tumor surgery due to their immunosuppressive properties and intense angiogenic potential, there are also publications suggesting that NSCLCs have tumor suppressive properties (65). Altman et al. In the experimental study in which they injected fluorescently labeled NSSCs in different ways (subcutaneously with the tumor cell, subcutaneously in a distant area, intravenously, in the acellular human dermal matrix away from the tumor) and evaluated the tumor volumes; They concluded that NSCLCs are retained in the wound microenvironment and do not contribute to the microenvironment of distant tumor cells (66).

CONCLUSION

YDKKHs attract the attention of plastic surgeons as well as other branches because they can be obtained easily and abundantly. However, most of the clinical publications on the subject are in the form of case series. In addition, there is no standardization regarding the usage patterns of the NSSCs obtained, the number of cells required for treatment, and the number of treatment sessions. Therefore, large, randomized, controlled studies are needed to support their clinical use.

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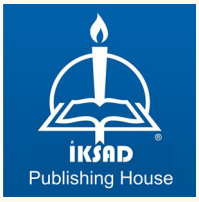

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